REMARKS

Claims 40-43 are pending in the instant application. Claims 40-43 have been rejected. Claims 40-43 have been amended. Support for these amendments is provided in the specification in Example 1 at pages 44-51 and more specifically at 50-51. No new matter is added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Obviousness-type Double Patenting Rejection

Claims 40-43 have been rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over claims 1-16 of U.S. Patent 6,365,151. The Examiner suggests that since the claims of the '151 Patent do not specifically exclude allogeneic cells or limit the cells to only autologous cells, the claims of the instant patent read on the '151 Patent. The Examiner suggests that the "allogeneic" cells fall within the scope of antigen presenting cells and fibroblast cells claimed in U.S. Patent 6,365,151.

Applicants respectfully traverse this rejection.

Allogeneic cells are defined at page 8, lines 21-26 of the instant patent application as cells derived from

organisms which are the same species of the host, but are not genetically identical. Further, claims 40-43 each specifically state that the cells of the instant invention are "allogeneic with respect to the host".

In contrast, claim 1-16 of the '151 Patent are drawn to a cellular immunogen and method for preparing and using a cellular immunogen comprising "host cells selected from the group consisting of professional antigen-presenting cells, fibroblasts and cells obtained from skin punch biopsy" (claim 1, col. 56, line 66 through col. 57, line 2) wherein the cells are excised from the host (see step (a) of claim 5) and then returned to the host following transfection (see step (c) of claim 9). Thus, contrary to the Examiner's suggestion, the allogeneic cells do not fall within the scope of antigen presenting cells and fibroblast cells of the '151 Patent which are explicitly taught to be excised from the host and then returned to the host.

Further, contrary to the Examiner's suggestion, all teachings of the specification of the '151 Patent relating to obtaining the host cells used in the claimed compositions actually do exclude allogeneic cells from the compositions. For example, col. 7, lines 18-30 of the '151 Patent teaches that:

> For those tumors showing proto-oncogene overexpression, this sequence homology permits application of the following strategy, which can be employed either prophylactically or therapeutically under conditions of cell-surface expression, or other forms of adjuvancity, as chosen to enhance immunogenicity: (a) immunization of host biopsied cells with a DNA construct comprising a transgene cognate to the target proto-oncogene, which transgene encodes a gene product which induces host immunoreactivity to host self-determinants of the product of the target proto-oncogene; (b) return of the transfected cells to the body of the host to obtain expression of the transgene in the host, and this immunity against the proto-oncogene product.

Further, at col. 19, line 51, through col. 20, line 7, the '151 Patent teaches that:

> The host cells which may be transfected to derive the cellular immunogens of the present invention must express class I MHC and be susceptible to isolation and culture. Fibroblasts express class I MHC and may be cultured. Other preferred host cells are bone-marrow derived antigen-presenting cells such as macrophages, follicular dendritic cells and Langerhans cells, for example. Primary skin fibroblasts may be obtained as follows. Accordingly punch biopsies of host human skin are performed to harvest fibroblasts. Punch biopsies can be performed by a competent physician as a standard clinical procedure . . .

Further, at col. 21, beginning at line 51 of the '151 Patent it is taught that the transfected cells are returned to the host to achieve vaccination. Specifically, it is taught that the cells may be reimplanted into the same body site from which they were originally harvested or may be restored to a different site.

Also see page 15, lines 1-10 of the instant application wherein differences between the instant vaccination strategy

and that disclosed in PCT/US97/00582, from which the '151 Patent claims benefit are set forth. As taught therein, the methodology taught in PCT/US97/00582 utilizes excised host cells for preparing the cellular immunogen. According to the present invention, the cellular immunogen is prepared from cells obtained from a donor other than the patient, and other than an identical twin of the patient. Hence, while PCT/US97/00582 and the '151 Patent describe inoculation constituting a syngeneic transfer, the present invention relies upon an allogeneic transfer.

Furthermore, and most importantly, the test in an obviousness-type double patenting rejection is not whether or not claims of the first issued patent "exclude" subject matter claimed in the instant application but rather whether the claims of the instant application define an invention that is merely an obvious variation of the invention claimed in the '151 Patent. See MPEP 804. A double patenting rejection of the obviousness-type is analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103. In re Braithwaite, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Thus, the analysis to be employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 determination. MPEP 804.

The '151 Patent neither teaches nor suggests use of cells allogeneic with respect to the host in their compositions. Thus, this reference neither teaches nor suggests limitations of the instant claimed invention, namely "a cellular immunogen comprising cells which are allogeneic with respect to the host." Further, the '151 Patent provides no reasonable expectation of success that compositions comprising allogeneic cells as opposed to host cells would be effective. Finally, the '151 Patent provides no motivation whatsoever to modify its teachings and utilize cells other than the disclosed host cells.

Thus, this reference in no way renders obvious claims of the instant application which are drawn not to compositions and method comprising host cells but rather to compositions and methods for preparing a composition comprising cells allogeneic with respect to the host.

Withdrawal of this obviousness-type double patenting rejection is therefore respectfully requested.

II. Rejection of Claims 40-43 under 35 U.S.C. 112, first paragraph

Claims 40-43 have been rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement. The Examiner suggests that the specification

does not provide an enabling disclosure for vaccinating any host against any disease associated with a proto-oncogene by the administration of a cellular immunogen transfected ex vivo with any transgene construct encoding any mutant proto-oncogene DNA. Further, the Examiner suggests that it would have required undue experimentation to practice the instant invention as claimed and the skilled artisan would not have predicted that any and all mammals could be vaccinated against cancer using the transgene constructs and transfected cells of the instant invention.

Applicants respectfully traverse this rejection.

At this point in the prosecution history of this case wherein Applicants have responded to 2 Office Actions, 2 Final Rejections and have filed 2 Requests for Continuation of Examination, it is believed that characterization of the invention by the Examiner should be correct. However, Applicants respectfully point out that the Examiner's characterization of the disclosure of the specification beginning at page 3 of this Office Action is incorrect. Contrary to the Examiner's suggestion, the specification does not disclose a cellular immunogen comprising "host cells transfected with a least one transgene . . . " but rather a cellular immunogen comprising cells allogeneic to the host. See the specification for example at page 12, lines 16-19 and page 15, lines 1-11. Also incorrect is the

Examiner's suggestion that the specification discloses a method of making a cellular immunogen comprising excising cells from a host and transfecting them with a transgene construct and methods of vaccinating a host against diseases comprising excising cells from a host, transfecting said cells with said transgene construct and reintroducing the cells to a host. A vaccination protocol is set forth in Example 2 at page 51 of the instant application and makes quite clear that the cells are obtained from a donor (other than the patient-to-be-treated or identical twin thereof). Further all pending claims are explicitly drawn to cellular immunogens and methods for preparing cellular immunogens comprising cells which are allogeneic with respect to the host.

Further, MPEP 2164 makes clear that the invention one skilled in the art must be enabled to make and use is that defined by the claims of the particular application. Thus, the Examiner's suggestion at page 4 of the Office Action that "the specification does not provide an enabling disclosure for vaccinating any host against any disease associated with the over expression of a proto-oncogene by the administration of a cellular immunogen transfected ex vivo with any transgene construct encoding any mutant proto-oncogene DNA" is irrelevant since the claims are not drawn to "any disease", "any transgene construct" or "any mutant

proto-oncogene". Instead, the claims of the instant application presently recite transfection with a vector comprising a non-transforming transgene cognate to a target proto-oncogene which is derived by deletion of a sequence of the transgene essential for transformation and consisting of wild-type sequence outside the deleted sequence, and a strong promoter to drive the expression of the cognate transgene in the transfected cells. Further, claims 40 and 41 specify that the target proto-oncogene is selected from the group consisting of AKT-*2*, *c-erbB-2* (HER2/*neu*), MDM-*2*, *c-myc*, *c-myb*, *c-ras*, *c-src and c-yes* and claim 42 and 43 specify that the target proto-oncogene is selected from the group consisting of *c-erbB-2* (HER2/*neu*), *c-myc* and *c-src*.

Also irrelevant to the instant claimed invention are the Examiner's concerns set forth at page 7 of the Office Action about the predictability of in vivo gene therapy. Claims of the instant application are drawn to a cellular immunogen comprising allogeneic cells clearly transfected ex vivo with respect to the host with the vector. Ex vivo transfection is a technique generally recognized in the art as more effective than in vivo transfection.

Further, while Applicants disagree with the Examiner's suggestion that immunization against cancer implies that the mammal is prevented from developing cancer upon administration of the immunizing compounds of the instant

invention, in an earnest effort to advance the prosecution of this case, Applicants have amended the claims in accordance with teachings of Example 1 at pages 40-51 to state that the cellular immunogen promotes tumor regression in a host.

At pages 4-5 of the Office Action, the Examiner has acknowledged the specification to provide several working examples of the instant claimed invention, and in particular three plasmids which encode v-src. The Examiner acknowledges that these working examples disclose that the subcutaneous injection in wings of chicken with any of the three src expressing plasmids resulted in tumors which appear to spontaneously regress over time. The Examiner also acknowledges that the working examples demonstrate that injection of 100 μg of v-src plasmid followed 5 weeks later by a second injection of 200 μg of c-src plasmid results in a decrease in the percentage of chickens with palpable tumors compared to control animals.

Thus, the specification, with its acknowledged working examples of three cellular immunogens, injection of which resulted in tumor regression over a period of weeks, clearly provides sufficient guidance to make and use cellular immunogens which promote tumor regression in a host as now claimed.

Withdrawal of this rejection under 35 U.S.C. 112, first paragraph is respectfully requested in light of the above remarks and the amendments to the claims.

III. Rejection of Claims 40-43 under 35 U.S.C. 102(e)

Claims 40-43 have been rejected under 35 U.S.C. 102(e) as being anticipated by Chada et al. (U.S. Patent 5,693,522). Applicants respectfully traverse this rejection.

To anticipate a claim, a reference must teach every element of the claim. See MPEP 2131.

Claims of the instant invention are drawn to a cellular immunogen comprising cells transfected with a vector comprising at least one non-transforming transgene cognate to a target proto-oncogene. The claims state that the non-transforming cognate transgene is derived by deletion of a sequence of the transgene essential for transformation and consisting of wild-type sequence outside the deleted sequence.

In contrast, Chada's constructs all require a mutation outside the deletion site, even where the construct is truncated to remove tumorigenicity. See specifically teachings in Chada at col. 2, line 61 through col. 3, line 8, col. 4, line 49 through col. 5, line 18 and col. 6, lines 54-60 wherein Chada explicitly teaches that the cellular

components were altered via mutation and that the immune response was directed against novel coding regions.

Accordingly, since Chada et al does not teach a non-transforming cognate transgene derived by deletion of a sequence of the transgene essential for transformation and **consisting of wild-type sequence outside the deleted sequence** as set forth in the instant claimed invention, this reference cannot anticipate the instant claimed invention.

Withdrawal of this rejection under 35 U.S.C. 102(e) is therefore respectfully requested.

IV. Rejection of Claims 40 and 42 under 35 U.S.C. 102(b)

Claims 40 and 42 have been rejected under 35 U.S.C. 102(b) as being anticipated by Gelman et al. (Oncogene 1993);8(11):2995-3004).

Applicants respectfully traverse this rejection.

As discussed in Section III, supra, to anticipate a claim, a reference must teach all of the elements of the claims. Claims of the instant invention are drawn to a cellular immunogen comprising cells transfected with a vector comprising at least one non-transforming transgene cognate to a target proto-oncogene, said non-transforming cognate transgene derived by deletion of a sequence of the transgene essential for transformation and consisting of wild-type sequence outside the deleted sequence.

In contrast, Gelman discloses vaccination of mice against avian viral v-src induced tumors with NIH3T3 and Balb/c3T3 cell lines expressing avian viral v-src, avian c-src, mutant avian viral 157src, mutant avian viral 1702src, and fusion protein of avian c-src protein tyrosine kinase domains and 157src or 1702src. None of the constructs taught by Gelman are deleted in the sequences necessary for transformation. In fact, the cell lines disclosed by Gelman exhibit a transforming phenotype. Further, Gelman teaches at pages 3001-3002 that cellular immunogens are effective in eliciting immune response only if transformed by src-specific sequences.

Thus, Gelman et al. clearly in no way teaches or suggests a vector comprising at least one **non-transforming transgene** cognate to a target proto-oncogene, said **non-transforming cognate transgene** derived by deletion of a sequence of the transgene essential for transformation and consisting of wild-type sequence outside the deleted sequence as claimed in the instant invention. Therefore this reference, which neither teaches nor suggests all the elements of the claimed invention, cannot anticipate the claimed invention.

Withdrawal of this rejection under 35 U.S.C. 102(b) is therefore respectfully requested.

V. Conclusion

Applicants believe that this submission overcomes all pending rejections in this case and comprises a full and complete response to the Office Action of record. Reconsideration and allowance of the pending claims is earnestly solicited in light of the above described amendments and remarks.

Respectfully submitted,

Kathleen A. Tyrrell
Registration No. 38,350

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LICATA & TYRRELL P.C.
66 E. Main Street
Marlton, New Jersey 08053

856-810-1515